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DIET AND SEX AS FACTORS IN CREATINURIA IN MAN

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BY

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B. S. Carleton College, 1912

THESIS

Submitted in Partial Fulfillment of the Requirements for the

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I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY

SUPERVISION BY Genevieve Stearns

ENTITLED Diet and Sex as Factors in Creatinuria in Man

BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR

THE DEGREE OF Master of Science

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____________________	on
____________________	Final Examination*

*Required for doctor's degree but not for master's

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General Introduction

The origin and fate of creatine in the human organism is one of the most interesting metabolic problems of today. While creatine is, in all probability, usually converted into creatinine in the body and excreted in this form, under certain conditions it may be excreted unchanged.

It is known that creatine is normally never excreted in the urine of adult men, while it may appear at irregular intervals in the urine of women. After prolonged fasting, in cases of hyperthyroidism, and in certain other pathological conditions, creatine may be found in the urine of both sexes. It occurs normally in the urine of women during the latter part of pregnancy and immediately after parturition. It is also usually present in the urine of young children, disappearing in the case of the male child at about the age of seven years, and continuing up to puberty in the female child.

The fate of creatine fed by mouth also varies with the age and sex of the subject. When fed to infants and young children, there is an almost quantitative elimination of unchanged creatine; in men, amounts up to 5 gms. may be ingested without the production of creatinuria and without increasing the output of urinary creatinine. No experiments dealing with the ingestion of

creatine by women could be found in the literature.

It is evident from the above facts that age and sex are important factors in influencing creatine excretion. Whether diet is also a factor is still an open question. Miss Denis has maintained that creatinuria in women is caused by a high protein diet; Mendel and Rose attribute it to a lack of carbohydrate in the diet; while Underhill, in his work on rabbits, concludes that there is a direct relationship between acidosis and creatine elimination.

From this brief resume, it may readily be seen that the problem is still unsettled and there is need of more experimental data on the subject.

Krause (1) in 1911, as a result of observations taken at irregular intervals, noted the fact that creatine often appeared in the urine of normal women and concluded from his experiments that creatine was associated with periodic variations of the sexual function, since it always appeared in urine directly after the menstrual period and was often present in the intermenstrual period.

For several years his results were accepted without question until M. S. Rose (2) in experiments with healthy women continuing thru periods of a month or more, was unable to confirm Krause's findings and concluded there was no direct relation between creatine output and the sexual cycle. She also con-

cluded that the amount of protein in the diet was not a causal factor as with her subjects diets resulting in the elimination of 20 grams of urinary nitrogen did not induce creatinuria where none previously existed, and diets low in protein did not decrease the amount of creatine in the urine, where it was continuously present. However Denis and Kramer (3) earlier in this same year found that the excretion of creatine in children varied directly with the amount of protein in the diet, and a few months later Denis and Minot (4) induced creatinuria in healthy women by the ingestion of diets rich in protein. Similar experiments with normal men gave negative results, as did also the experiments of Lewis and Doisy (5).

Rose, Dimmitt and Bartlett, (6) in 1918 found that increases of 300 - 400 per cent in protein intake were entirely without effect on excretion of creatine in either men or women. They were also unable to induce creatinuria by a fivefold increase in the calorific value of the diet, without increasing the protein, and therefore concluded that the creatine of the urine was wholly of endogenous origin.

In 1919, Gamble and Goldschmidt (7) showed that increase in the urinary creatine of infants on high protein diet was due largely to the creatine of the milk. As milk formed a considerable part of the high protein diets fed to

children by Denis and Kramer, it is possible that the rise in creatine excretion obtained was to be attributed not to protein as such, but to the creatine content of the milk.

In 1914, Krause (8) administered creatine to children and found that amounts as small as 0.1 gram caused an increase in the amount of creatine excreted. Powis and Raper (9) in 1916 confirmed these results.

Several investigators have administered creatine to men, either per os or parenterally, with various and rather conflicting results. Folin (10) states that in men on a low nitrogen diet, creatine in amounts less than 3 - 5 grams is completely retained by the body: Klercker (11) also found that small amounts of creatine were almost wholly retained, but amounts over 2 grams were excreted in part. Plimmer, Dick and Lieb (12) found that 2.5 grams of creatine must be ingested before it appeared in the urine, but Burns and Orr (13) observed a creatinuria after the ingestion of only 0.5 grams of creatine. Myers and Fine (14) ingested amounts of creatine varying from 1 - 5 grams with the recovery of 20 - 25 per cent from one gram and nearly 40 per cent from 5 grams of ingested creatine. Rose and Dimmitt (15) administered creatine in quantities up to 20 grams with the recovery of nearly 60 per cent from the larger amounts ingested. When the quantities administered were less than 2 grams, only about

5 per cent was recovered.

Lyman and Trimble (16) administered creatine parenterally in amounts up to 1.05 grams and obtained only 4 per cent of it as urinary creatine, while 20 per cent was recovered from the urine as creatinine. Thus, even when it is so administered that there is no chance for bacterial action in the intestine (Twort and Mellanby (17)), creatine introduced into the body seems to be retained in large part by the body tissues.

No experiments dealing with the ingestion of creatine by women could be found in the literature. The experiments reported in the present study were undertaken to afford additional evidence on the following points, since the experimental data bearing upon them seemed to be conflicting and in many cases improperly controlled.

1. The relation of creatinuria to the sexual cycle in the normal adult female.
2. The influence of diet on the creatinuria of women.
3. The ability of the female organism to destroy creatine administered per os. Is the destruction or transformation of ingested creatine by the female influenced by variations in the sexual functions?

Experimental Methods and Data.

The subjects of the following experiments were healthy young women, graduate assistants in this university, engaged in their regular routine during the period covered by the experiments. Subject E.M.A. suffered from physical overstrain accompanied by a slight tendency toward hyperthyroidism during the first experimental period but had completely recovered at the time of the later experiments. The other subjects were in good health thruout.

The diets, which were both meat and milk free, were not weighed but were approximately uniform from day to day. The low protein diets consisted chiefly of potatoes, supplemented by bread and butter, fruit and green vegetables. The high protein diet of the earlier experiments consisted mainly of eggs, with beans, bread and butter, while in the later experiments the protein was supplied by a commercial diabetic food (1), which was made into muffins. This was supplemented by cheese and legumes. The daily consumption of food in the high protein period was not as constant as in the low, an attempt being made to secure a maximum excretion of nitrogen.

1. Glidine, a commercial "pure vegetable protein food prepared wholly from wheat." The preparation used in these experiments contained 15.1 per cent nitrogen. According to the analysis of Street (Connecticut Agric. Exp. Station, Ann.Rep., 1913, 25) glidine contains no starch and 91.4 per cent protein.

The creatine was a Kahlbaum preparation and the creatinine was made in this laboratory.

Folin's[1] microcolorimetric method was used for the determination of creatinine, and Benedict's[2] modification of the Folin method for creatine. Total nitrogen was determined by the Kjeldahl-Gunning method and the hydrogen ion concentration according to the method of Henderson and Palmer.[3] Toluene was used as a preservative. The experiments recorded in tables I and II were carried out at the same time and under uniform conditions. It is perhaps a significant fact that these experiments were undertaken near the close of an unusually difficult year of teaching and study, attendant upon confused conditions of 1918-19. A comparison of the results of these experiments with later ones (Tables VI and VII) with the same subjects and the same type of diet, but after the summer's vacation, shows rather striking differences in the frequency of the occurrence of creatine in the urine.

In these earlier experiments the high protein diets could not be maintained for as long a period since the warm weather made continued ingestion

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1.Folin,J.Biol. Chem., XVII, 469.

2.Benedict,J.Biol. Chem., XVII, 191.

3.Henderson and Palmer,J. Biol. Chem., XIII, 393.

of such diets difficult.

A further study (Table III) was carried out to obtain additional evidence concerning the relationship of the menstrual period to creatinuria. The diet was low in protein and approximately constant. The experiment covers two successive menses with the whole of the intervening period.

The fate of creatine administered per os was also studied during this experiment, three doses of approximately 0.5 grams each of creatine, and one dose of 0.5 gram of creatinine being ingested at intervals.

Additional data are presented in Tables IV and V on the creatinuria of the menstrual period, with two other subjects. The last three experiments (Tables VI, VII, VIII), in two of which the subjects were the same individuals as in the earlier experiments (Tables I and II), are also parallel in period of time. These furnish data concerning the effect of various diets upon creatine excretion both during the menstrual and intermenstrual periods, and give additional evidence regarding the fate of ingested creatine.

Subject R.M.A. was unable to continue the high protein diet over as long a period as the other two women. The periods of high milk diet in these experiments were carried out to determine whether, when milk was consumed in such large quantities, its creatine acted as a stimulus for the excretion of

endogenous creatine. It is unfortunate that these periods were of such brief duration that the results are necessarily inconclusive.

Discussion

A. Relation of Creatinuria to the Menstrual Cycle

According to Krause (1), creatine normally disappears from the urine of women with the onset of the menstrual period, reappearing immediately afterward and may or may not be present during the intermenstrual period. His experiments are open to the criticism that his analyses were made at irregular intervals sometimes a month or more apart, very rarely two days in succession. It does not seem that data compiled in this manner give a sufficient foundation for such far-reaching conclusions as are drawn.

The results given in the foregoing tables afford data obtained from five subjects under carefully controlled conditions, and include the complete menstrual period with fore and after periods in seven cases, partial data in two others. Table III gives data covering two successive menses with the whole of the intermenstrual period. For one subject (G. S.) the data include four complete menstrual periods.

To summarize briefly the findings:

In two experiments only was creatine present just before the onset of the menses;

in five (leaving out of consideration the days in which creatine was ingested), it occurred during the period; and in only one was a creatinuria observed directly after menstruation; at no time was a tendency toward creatinuria more marked during or near the menstrual period than at any other time. In fact excepting in the first two experiments (Tables I and II) which will be considered later, creatinuria was not only rare and of very brief duration when it occurred, but the amounts of creatine excreted were very small, seldom over 100 milligrams.

As these experiments were carefully controlled and afford complete data over comparatively long periods of time and with different subjects, the results justify the conclusion that the menstrual period can bear no direct relation to the appearance of creatine in the urine of women. This conclusion is in harmony with the more recent work on this subject. (2,6).

B. Influence of the Protein Content of the Diet on Creatine Excretion

(1) Low Protein

In a survey of the low protein periods the most striking fact, as has been noted before, is the frequency of creatinuria in the earlier experiments and the large amounts of creatine excreted in these, compared with the almost negligible amounts observed in the later experiments. A comparison of the low protein periods of the experiments illustrated in Tables I, III, and VI, in which

the same individual served as subject, will illustrate this point. In the first experiment with a total of fourteen days, creatine appears in the urine five times in four of which the amount eliminated is above 100 milligrams, the maximum being over 300 milligrams (May 8th). In experiment III which covers a period of thirty-five days, it is excreted only three times, exclusive of its elimination after creatine ingestion, and only once does the excretion rise above 100 milligrams. In the thirteen days comprising the low protein period of experiment VI creatinuria occurs only once, on the first day (140 milligrams).

Comparing in like manner the two experiments in which R. M. A. served as subject (II and VII) in which the low protein periods were of equal duration (twenty-three days), it is seen that in the earlier experiment, creatine appears seven times in amounts varying from 31-271 milligrams, the average being 112 milligrams; in the later experiment, exclusive of its excretion following creatine ingestion, it appears only once (110 milligrams).

(2) High Protein

In the high protein periods the results are even more variable. In experiment I the high protein diet seemed at first to cause a creatinuria, but even with a continued rise of the urinary nitrogen, creatine disappeared entirely from the urine, suggesting perhaps that the organism can adjust itself to a

higher protein level. In experiment II small amounts of creatine were excreted daily for the first five days, but on the sixth, the urine was creatine free, although the urinary nitrogen for that day was higher than during the first part of the period.

In the second series of high protein periods (Tables VI, VII, and VIII), during experiment VI creatine appeared in the urine only on the seventh day, although the urinary nitrogen reached a figure more than three times that of the low protein period immediately proceding. The high protein period of experiment VII covered such a short time that the urinary nitrogen did not reach a level high enough to be significant. In experiment VIII there was an intermittent creatinuria, the creatine excreted never exceeding 100 milligrams.

In these experiments none of the subjects was able to maintain an excretion of urinary nitrogen above 20 grams for a period of several days, as was done by one of Miss Denis' subjects (18). Our high protein periods also followed periods of low protein diet which Miss Denis states retards the production of creatinuria. However one subject (G. S.) maintained for a period of eight days a nitrogen excretion averaging nearly three times that of the preceding low protein period, yet creatine was only excreted twice, and then in amounts very much smaller than those recorded by Miss Denis. The results recorded in this paper

are more in harmony with those of Mrs. Rose,(2) and of Rose,Dimmitt and Bartlett (6), who state that high protein diet fails to induce the excretion of creatine in normal men and women.

The results given in Tables VI and VIII indicate also that there is no more tendency toward creatinuria during a menstrual period when the diet is high in protein than when it is low; in fact, in experiment VI, during the high protein period there was a total absence of creatinuria during and after the menses.

(3) High Protein diets derived from Milk

An attempt was made to study the effect of the ingestion of large quantities of milk on the production of creatinuria. L. R. ingested three quarts of milk daily for two days (on the first of which the diet was not otherwise creatine free) and on the third day increased this quantity to five quarts. R. M. A. consumed three quarts of milk the first day of the experiment and five and one-half quarts the second. As the total amount of protein consumed per day in these experiments did not exceed that of the high protein periods, the production of creatinuria could not be attributed to protein alone.

Gamble and Goldschmidt (7) claim that with infants, an increase in the protein of the diet effected by increasing the amount of milk ingested, causes a

rise in urinary creatine due, not to the protein, but to the creatine content of the milk. Assuming that the figures obtained by Denis and Minot (19) for the creatine content of cow's milk are correct, the amount is so small - 25 milligrams per liter - that even five quarts would yield only 125 milligrams which, in order to obtain the amounts excreted by R. M. A. ,would have to be eliminated in toto. This does not seem probable in view of the small percentage of ingested creatine which could be recovered in the urine in experiments to be discussed later.

There is a possibility that creatine of milk may be "protected" from bacterial action in the intestine; or that it may act as a stimulus for the overproduction and consequent excretion of endogenous creatine; or that the ingestion of such large volumes of liquid may produce a strain on the system causing an excretion of creatine. This last view seems the most tenable, but the period of the diets was too brief to permit of definite conclusions.

C. Fate of Creatine Administered *per os*.

As shown in Table III, after 0.494 gram of creatine was ingested on July 2nd, during a menstrual period, 550 miooigrams* were excreted the same day and 60 milligrams on the following, making a total of 710 milligrams, or more than 200 milligrams above the amount ingested. The dose was repeated on July 7th, during the intermenstrual period, followed neither by an excretion of creatine in the urine nor by a rise in urinary creatinine; on July 22nd, 0.5 gram of creatinine ingested, resulted in the recovery of approximately 50 per cent in the urine. During the succeeding menstrual period 0.5 gram of creatine was again administered but this time there was no resulting creatinuria, nor was the urinary creatinine increased.

During experiment VII, on November 3rd, 0.5 gram of creatine was ingested and 50 milligrams were recovered in the urine; on November 16th, 2.0 grams of creatine and 0.5 grams of creatinine *per os* caused an excretion of 310 milligrams of creatine with practically no change in the urinary creatinine. On November 21st, 1.0 gram of creatine was ingested in two doses, so as to minimize the possibility of bacterial decomposition, but only 160 milligrams were recovered in the urine.

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*The creatine excreted in the urine was calculated as creatinine.

Likewise in experiment VI, one gram of creatine ingested on November 18th resulted in the recovery of only 24 milligrams. On November 20th, one gram of creatine was administered in divided doses of approximately 100 milligrams each to facilitate absorption, but only 30 milligrams were excreted in the urine.

According to Twort and Mellanby (17), creatine may be destroyed in the intestine through bacterial action. This, of course, is a possibility but it does not seem sufficient to account for all the loss, for when creatine was administered when the stomach was empty and the probable rate of absorption much increased, the amounts recovered in the urine were not appreciably larger than those obtained when creatine was ingested after a meal.

In general, the results of these experiments upon women are parallel to those of similar experiments upon men. Creatine administered *per os* in small amounts rarely reappears in the urine and even in amounts of 1-2 grams causes only a slight creatinuria. There seems to be, therefore, no difference in the assimilation and retention of creatine by men and women when administered *per os*.

The excretion of creatine during periods of high milk diet will bear further investigation.

D. Relation of Creatinuria to the Physical Condition of the Subject

In seeking a possible cause of the excretion of creatine, the striking differences between the creatinurias evidenced by experiments I and II, on the one hand, and VI and VII on the other, seemed to afford an explanation. As previously stated, both subjects were in poor physical condition during experiments I and II. The week of May 10-18th, in particular, was one of physical and nervous strain, and in both cases, but especially with R. M. A., there was marked creatinuria. In contrast to the frequent occurrence of creatine in these experiments, is its almost entire absence in experiments III, VI, and VII, where the subjects were in much better physical condition.

Throughout the course of the experiments it was noted that unusual physical exertion or nervous strain was often accompanied by an excretion of creatine. It seems at least possible also, that the creatinuria of the first days of the high protein periods might have been due to the physical strain attendant upon such a diet. This explanation is borne out by the gradual disappearance of the creatinuria as the subject became accustomed to the diet.

It would be interesting to compare the prevalence of creatinuria among healthy women who lead an outdoor life with light physical labor and women who work indoors under high nervous tension.

Summary.

From the data obtained from experiments on five healthy young women over periods of time varying from five to thirty-five days, the following conclusions were reached:

1. There is no direct relation between the phases of the menstrual cycle and the appearance of creatine in the urine.

2. Protein, per se, is not a causal factor in the production of creatinuria and there is no more tendency toward the production of creatinuria by high protein diets during the menstrual than in the intermenstrual periods.

3. The retention of ingested creatine by women is not markedly different from that by men.

4. The general physical condition of the subject has more apparent influence on the production of creatinuria in women than any other factor considered in this study.

Table I

Subject C.S. Wt. 56 Kgm.

Date	Preformed Creatinine gm.	Total Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	P^{H^+}
Period I Low Protein diet.					
May 7	1.071	1.071	—	4.62	6.63 - 7.0
" 8	0.84	1.023	0.183	6.72	7.0 - 7.4
" 9*	1.10	1.10	—	6.00	7.4 - 7.6
" 10*	1.18	1.18	—	5.81	7.0 - 7.4[2]
" 11*	0.84	0.84	—	4.18	5.92 - 6.23[3]
" 12*	1.16	1.16	—	7.25	6.63 - 7.0
" 13*	1.04	1.04	—	5.50	6.63 - 7.0
" 14	0.75	1.07	0.32	5.74	6.63 - 7.0[1]
" 15	1.10	1.10	—	6.50	6.63 - 7.0[1]
" 16	0.975	1.13	0.16	7.58	6.63 - 7.0[1]
" 17	1.08	1.18	0.10	5.94	6.63 - 7.0[1]
" 18	1.08	1.08	—	5.09	6.63 - 7.0
" 19	0.97	1.01	0.04	6.31	6.63 - 7.0
" 20	1.02	1.02	—	5.60	6.63 - 7.0
Period II High Protein diet.					
May 21	1.10	1.10	—	5.70	6.63 - 7.0
" 22	0.80	0.80	—	5.80	6.23 - 6.63
" 23	1.03	1.03	—	7.22	5.45 - 5.92
" 24	1.03	1.12	0.09	9.59	6.23 - 6.63
" 25	1.02	1.08	0.06	9.66	5.45 - 5.92
" 26	1.02	1.15	0.13	12.27	5.45 - 5.92
" 27	1.12	1.12	—	13.46	5.92 - 6.23
" 28	0.98	0.98	—	13.82	5.45 - 6.23

Table I
(Continued)

Date	Preformed Creatinine gm.	Total Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	pH
May 29	1.12	1.12	—	13.85	5.45 - 5.92
" 30	1.12	1.12	—	12.90	5.45 - 5.92

* Menstrual period.

1. Overwork and resulting nernous strain.

2. Over twenty-four hours.

3. Under twenty-four hours.

Table II

Subject R.M.A. Wt 57 kg.

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	$P_{H^{+}}$
Period I	Low Protein diet				
May 7	1.08	1.08	-	4.90	5.92 - 6.23
8	0.75	0.75	-	3.20	6.63 - 7.00°
9	1.04	1.04	-	6.70	6.63 - 7.00
10	1.04	1.18	0.14	5.26	6.63 - 7.00[1]
11	0.84	0.94	0.10	3.56	5.42 - 5.92[1]
12	1.31	1.31	-	6.82	6.23 - 6.63[1]
13 and 14		..	(no collection)	..	.. ..
15	0.94	1.21	0.27	6.26	5.92 - 6.23[1]
16	0.90	0.90	-	6.97	6.23 - 6.63[1]
17	1.04	1.04	-	5.10	6.23 - 6.63[1]
18	1.08	1.13	0.05	5.97	6.23 - 6.63[1]
19	1.04	1.21	0.17	6.85	6.63 - 7.00
20	1.04	1.04	-	5.90	6.63 - 7.00
21	1.04	1.04	-	5.60	6.63 - 7.00
22	1.04	1.07	0.03	5.85	6.63 - 7.00
23	1.16	1.16	-	5.18	6.23 - 6.63
24	1.16	1.16	-	6.82	6.63 - 7.00
25*	1.02	1.02	-	4.77	5.92 - 6.23
26*	1.13	1.13	-	4.05	5.92 - 6.23
27*	1.13	1.13	-	6.77	5.92 - 6.23
28*	1.02	1.08	0.06	5.70	5.92 - 6.23
29	1.10	1.10	-	6.40	6.23 - 6.63

Table II (Continued)

Subject R.M.A. Wt 57 kg

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	p^{H^+}
Period II	High Protein diet				
May 30	1.02	1.13	0.11	7.15	5.45 - 5.92
31	0.98	1.02	0.04	7.11	5.92 - 6.23
June 1	1.02	1.07	0.05	8.63	6.23 - 6.53
2	1.07	1.12	0.05	6.60	5.45 - 5.92
3	1.14	1.21	0.07	10.56	6.23 - 6.53
4	1.08	1.08	-	7.37	5.92 - 6.23

* menstrual period

° incomplete collection

1.illness, overstrain

Table III

Subject G. S. Wt 56 Kg

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	P^{H+}
Period I Low Protein diet					
June 26	1.03	1.03	-	5.89	6.63 - 7.00
27	1.04	1.04	-	5.18	6.23 - 6.63
28	0.24	0.24	-	-	- - °
29*	0.49	0.49	-	-	- - °
30*	0.90	0.94	0.04	4.55	6.23 - 6.63
July 1*	0.90	0.90	-	4.94	5.45 - 5.92
2*	1.08	1.63	0.55	6.43	5.92 - 6.23[1]
3*	1.08	1.14	0.06	6.33	6.63 - 7.00
4	1.10	1.10	-	6.21	6.63 - 7.00
5	1.12	1.12	-	6.71	6.23 - 6.63
6	0.94	0.94	-	5.90	6.63 - 7.00
7	0.99	0.99	-	5.23	6.23 - 6.63[2]
8	1.05	1.05	-	5.20	6.23 - 7.00
9	1.07	1.07	-	5.10	6.63 - 7.00
10	0.95	0.95	-	4.40	6.63 - 7.00
11	0.97	0.97	-	5.10	7.00 - 7.40
12	1.07	1.07	-	5.66	6.23 - 6.63
13	0.89	0.89	-	5.43	6.63 - 7.00
14	1.07	1.07	-	5.33	6.63 - 7.00
15	1.07	1.07	-	4.83	6.63 - 7.00
16	1.05	1.05	-	6.00	6.63 - 7.00
17	1.03	1.03	-	5.45	6.63 - 7.00
18	1.07	1.07	-	5.20	6.63 - 7.00

Table III (Continued)

Subject G. S. Wt 56 kg

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	p^{H^+}
July 19	1.11	1.11	-	5.18	6.23 - 6.63
20	0.92	0.92	-	4.52	6.23 - 6.63
21	1.03	1.03	-	5.08	6.23 - 6.63
22	1.39	1.39	-	4.92	7.00 - 7.40 [3]
23*	1.07	1.185	0.115	5.66	6.63 - 7.00
24*	0.92	0.92	-	5.02	7.00 - 7.40
25*	1.07	1.07	-	4.78	6.63 - 7.00 [4]
26*	1.01	1.01	-	5.15	6.63 - 7.00
27*	1.01	1.10	0.090	5.88	6.63 - 7.00
28*	1.04	1.04	-	5.44	6.63 - 7.00
29	1.05	1.05	-	4.90	7.00 - 7.40
30	1.04	1.04	-	5.27	6.63 - 7.00

* menstrual period

° incomplete collection

1.0.494 gm creatine per os.

2.0.502 gm creatine per os.

3.0.498 gm creatinine per os.

4.0.500 gm creatine per os.

Table IV

Subject H. R. Wt 47.3 kg

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	P^{H+}
July 12*	1.25	1.34	0.09	9.43	6.23 - 6.63[1]
13*	0.77	0.79	0.02	5.83	6.23 - 6.63
14*	0.88	0.88	-	7.96	6.63 - 7.00
15*	0.84	0.92	0.08	6.17	6.23 - 6.63
16*	0.82	0.82	-	6.02	6.63 - 7.00
17	0.90	0.90	-	5.16	6.23 - 6.63
18	0.92	0.92	-	7.18	6.23 - 6.63
19	0.92	0.92	-	9.38	5.92 - 6.23
20	0.68	0.68	-	4.28	6.23 - 6.63

* menstrual period

[1] diet not creatine free

Table V

Subject M. S. Wt 60 kg

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	P^{H+}
July 14	1.13	1.13	-	6.46	6.23 - 6.63
15	1.15	1.15	-	7.75	6.23 - 6.63
16	1.06	1.06	-	7.16	6.23 - 6.63
17*	0.96	0.96	-	6.95	5.92 - 6.93
18*	1.21	1.21	-	7.07	6.63 - 7.00

* menstrual period

Table VI

Subject G. S. Wt 56.7 kg.

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total No. gm.	P^{H^+}
Period I Low protein diet					
Oct. 24	1.15	1.29	0.14	7.55	7.00 - 7.40
25	0.97	0.97	-	5.18	6.63 - 7.00
26	1.06	1.06	-	6.96	7.40 - 7.60
27	1.08	1.08	-	5.45	6.63 - 7.00
28	1.02	1.02	-	6.27	7.00 - 7.40
29	1.02	1.02	-	5.71	6.63 - 7.00
30	1.12	1.12	-	7.09	6.63 - 7.00
31	-	-	-	-	- -
Nov. 1	1.12	1.12	-	5.88	6.63 - 7.00
2	0.96	0.96	-	5.43	7.00 - 7.40
3	1.02	1.02	-	5.62	6.63 - 7.00
4	1.04	1.04	-	5.55	6.23 - 6.63
5	1.08	1.08	-	-	6.63 - 7.00
Period II High Protein diet					
6	1.04	1.04	-	7.37	6.63 - 7.00
7*	1.08	1.08	-	15.56	6.63 - 7.00
8*	0.93	0.93	-	16.75	5.45 - 5.93
9*	1.07	1.07	-	13.57	5.45 - 5.93
10*	1.06	1.06	-	16.50	6.23 - 6.63
11	0.97	0.97	-	14.26	6.63 - 7.00
12	0.99	1.01	0.02	20.34	6.63 - 7.00
13	0.96	1.02	0.06	16.81	5.45 - 5.92

Table VI (Continued)

Subject G. S. Wt. 56.7 kg.

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	P^{H^+}
Nov. 14	1.15	1.16	-	19.60	6.23 - 6.63
15	1.04	1.04	-	14.74	6.23 - 6.63
16	0.99	0.99	-	10.46	6.63 - 7.00
17	0.95	0.95	-	11.20	6.63 - 7.00
Period III Low Protein diet					
18	1.056	1.08	0.024	12.68	6.63 - 7.00[1]
19	1.05	1.05	-	10.52	6.63 - 7.00
20	1.15	1.18	0.030	8.76	7.00 - 7.40[2]
21	1.17	1.17	-	8.25	7.00 - 7.40

* menstrual period.

1. 1.0 gm creatine per os.

2. 1.0 gm creatine per os. in divided doses

Table VII

Subject R.M.A. Wt. 65 kg.

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	$P^{H\,+}$
Period I	Low Protein diet				
Oct. 25	1.19	1.19	-	5.71	6.23 - 6.63
26	1.06	1.17	0.11	6.99	5.92 - 6.23
27	1.24	1.24	-	6.04	6.23 - 6.63
28	1.16	1.16	-	6.66	6.63 - 6.70
29	1.17	1.17	-	6.15	5.92 - 6.23
30	1.19	1.19	-	6.36	5.45 - 5.92
31	0.77	0.77	-	-	- - ^{0}
Nov. 1*	1.05	1.05	-	-	- - ^{0}
2*	0.91	0.91	-	4.12	7.00 - 7.40
3*	1.11	1.16	0.05	5.73	5.42 - 5.92 ^{1}
4*	0.90	0.90	-	5.44	6.30 - 7.00
Period II	High Protein diet				
5	1.12	1.12	-	4.35	6.23 - 6.63
6	1.04	1.04	-	5.93	6.63 - 7.00
7	1.15	1.15	-	11.08	6.63 - 7.00
8	1.07	1.07	-	10.20	5.45 - 5.92
9	1.08	1.08	-	8.05	5.92 - 6.23
Period III	Low Protein diet				
10	1.08	1.08	-	8.62	5.45 - 5.92
11	1.13	1.13	-	9.03	6.23 - 6.63
12	1.05	1.05	-	7.15	6.23 - 6.63

Table VII (Continued)

Subject R.M.A. Wt. 65 kg.

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	p^{H^+}
Period III	Low Protein diet				
Nov. 13	1.12	1.12	-	7.50	5.92 - 6.23
14	1.17	1.17	-	7.20	6.23 - 6.63
15	1.18	1.18	-	6.93	6.23 - 6.63
16	1.21	1.52	0.31	5.64	6.63 - 7.00 [2]
Period IV	Milk diet				
17	1.12	1.22	0.10	9.36	6.23 - 6.63
18	1.11	1.24	0.13	15.38	6.23 - 6.63
Period V	Low Protein diet				
19	1.02	1.02	-	9.38	6.63 - 7.00
20	1.09	1.09	-	6.99	6.63 - 7.00
21	1.11	1.27	0.16	7.26	6.63 - 7.00 [3]

* menstrual period

° incomplete collection

1. 0.5 gm creatine per os.

2. 2.0 gm creatine and 0.5 gm creatinine per os.

3. 1.0 gm creatine per os. in 0.5 gm doses

Table VIII

Subject L.R. Wt. 51 kg.

Date	Preformed Creatinine gm.	Total as Creatinine gm.	Creatine as Creatinine gm.	Total N. gm.	P^{H} +
Period I	High Protein diet				
Nov. 7	0.88	0.88	-	12.21	7.00 - 7.40
8	0.91	1.01	0.10	13.80	5.45 - 5.92
9	0.82	0.89	0.07	8.07	7.00 - 7.40
10	0.90	0.90	-	11.52	6.23 - 6.63
11*	0.88	0.88	-	13.28	6.63 - 7.00
12*	0.87	0.90	0.03	13.86	6.63 - 7.00
13*	0.84	0.84	-	11.36	5.92 - 6.23
14*	0.88	0.88	-	11.32	6.23 - 6.63
15	0.92	0.92	-	9.65	6.63 - 7.00
Period II	Milk diet				
16	0.84	1.04	0.200	9.3	7.00 - 7.40°
17	0.89	0.92	0.03	12.71	7.00 - 7.40
18	0.90	0.90	-	16.67	6.63 - 7.00

* menstrual period

° diet not meat free

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